

10/028,224

10/143,502

Page 4

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containing 1 : 7 : 13 :

Match level :

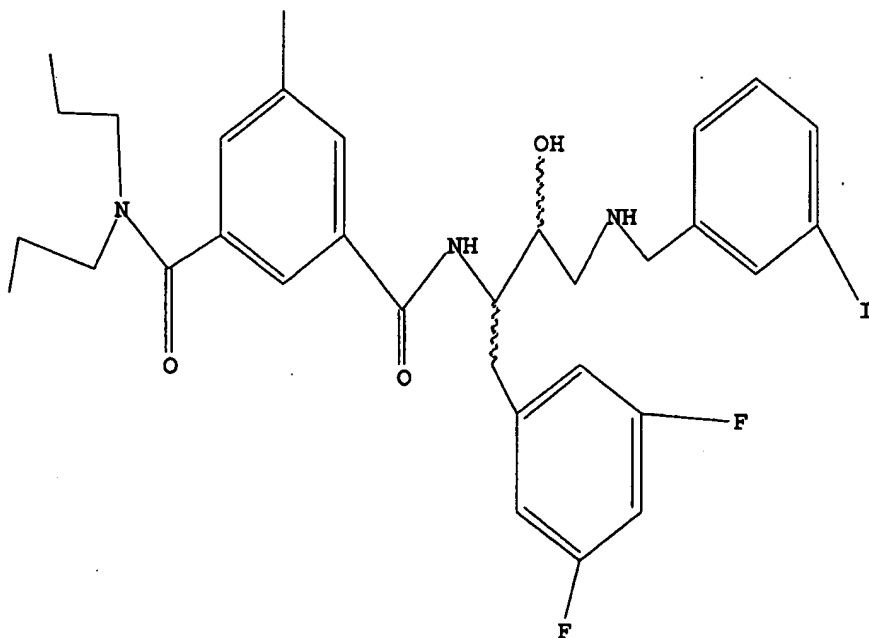
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11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS  
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS  
36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 11:37:22 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED  
SEARCH TIME: 00.00.04

2 ITERATIONS

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 2 TO 124  
PROJECTED ANSWERS: 0 TO 0

David

05/11/2006

L2 0 SEA SSS SAM L1

=&gt; s l1 sss full

FULL SEARCH INITIATED 11:37:35 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 38 TO ITERATE

100.0% PROCESSED 38 ITERATIONS

4 ANSWERS

SEARCH TIME: 00.00.01

L3 4 SEA SSS FUL L1

=&gt; file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

166.94

167.15

FILE 'CAPLUS' ENTERED AT 11:37:43 ON 11 MAY 2006

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FILE COVERS 1907 - 11 May 2006 VOL 144 ISS 20

FILE LAST UPDATED: 10 May 2006 (20060510/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

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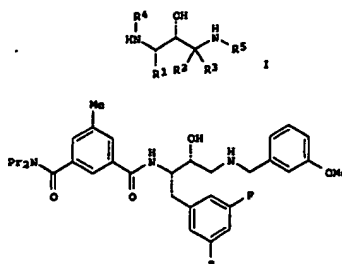
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 ACCESSION NUMBER: 2003:696859 CAPLUS  
 DOCUMENT NUMBER: 139:230480  
 TITLE: Preparation of substituted amine prodrugs useful in treating Alzheimer's disease  
 INVENTOR(S): Varghese, John; Jagodinska, Barbara; Maillard, Michel; Beck, James P.; Tenbrink, Ruth E.; Getman, Daniel  
 PATENT ASSIGNEE(S): Elian Pharmaceuticals, Inc., USA; Pharmacia & Upjohn  
 SOURCE: PCT Int. Appl., 483 pp.  
 CODEN: P1XXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NO 2003072535	A2	20030904	NO 2002-US7287	20030227
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RM:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TG, TZ, UG, ZM, ZW, AM, AZ, BY, RU, KE, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LJ, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, GQ, ML, MR, NE, SN, TD, TO			
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AU 2003225730	A1	20030909	AU 2003-225730	20030227
EP 1503980	A2	20050209	EP 2003-743271	20030227
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, SK, HU, SK			
BR 2003007998	A	20050628	BR 2003-7998	20030227
JP 2005519083	T3	20050630	JP 2003-571242	20030227
NO 200404046	A	20041115	NO 2004-4046	20040924
PRIORITY APPL. INFO.:			US 2002-359953P	P 20020227
			NO 2002-US7287	W 20030227

OTHER SOURCE(S): MARPAT 139:230480  
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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS ON STN (Continued)



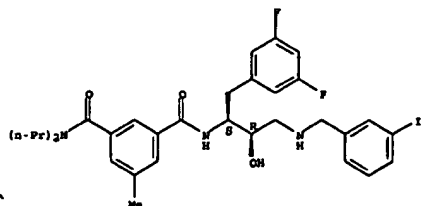
AB Amines [I]; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = N, (un)substituted alkyl, alkenyl, etc.; R3 = N, (un)substituted alkyl, alkenyl, etc.; R4 = XR, X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indenyl, etc.; R5 = (un)substituted alkyl, (CH2)6-3-cycloalkyl, etc.; e.g. N1-((1S,2R)-1-((3,5-difluorobenzyl)-2-hydroxy-3-((3-methoxybenzyl)amino)propyl)-5-methyl-N3,N3-dipropylisophthalamide), useful in treating Alzheimer's disease and other similar diseases, were prepared. Although the methods of preparation are not claimed, hundreds of example preps. are included. Thus, reacting (2R,3S)-3-amino-4-((3,5-difluorophenyl)-1-((3-methoxybenzyl)amino)-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-((1S,2R)-1-((3,5-difluorobenzyl)-2-hydroxy-3-((3-methoxybenzyl)amino)propyl)-5-methyl-N3,N3-dipropylisophthalamide). The compds. I exhibit an IC50 of < 50 µM against β-secretase.

IT 388063-46-SP, N-((1S,2R)-1-((3,5-difluorobenzyl)-2-hydroxy-3-((3-iodobenzyl)amino)propyl)-5-methyl-N',N'-dipropylisophthalamide 388065-47-SP, N-((1S,2R)-1-((3,5-difluorobenzyl)-2-hydroxy-3-((3-iodobenzyl)amino)propyl)-5-ethynyl-N',N'-dipropylisophthalamide RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RM 388063-46-5 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-5-methyl-N,N-dipropyl-(SC1) (CA INDEX NAME)

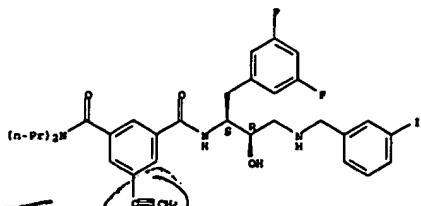
L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS ON STN (Continued)

Absolute stereochemistry.



RM 388065-47-2 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-5-ethynyl-N,N-dipropyl-(SC1) (CA INDEX NAME)

Absolute stereochemistry.



IT 388065-41-7, N-((1S,2R)-1-((3,5-difluorobenzyl)-2-hydroxy-3-((3-iodobenzyl)amino)propyl)-5-methyl-N',N'-dipropylisophthalamide trifluoroacetate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RM 388065-41-7 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-5-methyl-N,N-dipropyl-, mono(trifluoroacetate) (salt) (SC1) (CA INDEX NAME)

CN 1

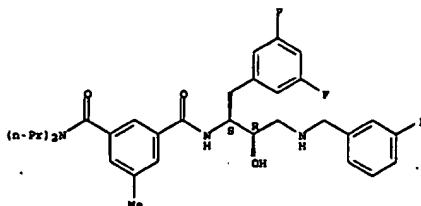
CRM 388063-46-5

David

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS ON STN (Continued)

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Absolute stereochemistry.



CN 3

CRM 76-05-1  
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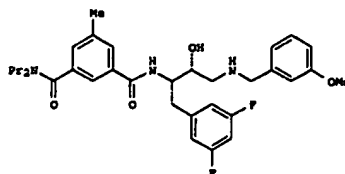
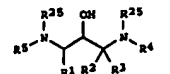
05/11/2006

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM  
 ACCESSION NUMBER: 2003:412801 CAPLUS  
 DOCUMENT NUMBER: 139:245782  
 TITLE: Preparation of M,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease  
 INVENTOR(S): Varghese, John; Mailard, Michel; Jagodinska, Barbara; Beck, James P.; Gailunas, Andrew; Fang, Larry; Seely, Jennifer; Tenbrink, Ruth; Fraskos, John;  
 PATENT ASSIGNEE(S): Mickelson, John; Samala, Lakshman; Hom, Roy  
 SOURCE: PCT Int. Appl., 1243 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-KA36072	20021108
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PRIORITY APPL. INFO.:				
US 2001-337122P P 20011108				
US 2001-344086P P 20011228				
US 2002-345635P P 20020103				
WO 2002-US36072 A 20021108				

OTHER SOURCE(S): MARPAT 139:245782  
 GI

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM (Continued)



AB The title compds. (I; R1 = (unsubstituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R3 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2;

R6 = (un)substituted Ph, naphthyl, indanyl, etc.; R25 = H, alkyl, alkoxy, etc.) which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared e.g., a multi-step synthesis of (1S,2R)-11,

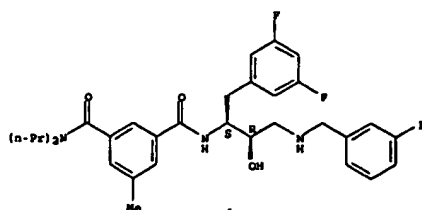
starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of

1-3 series.  
 IT 388063-46-5 388086-41-7 597562-84-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (Preparation of M,N'-substituted-1,3-diamino-2-hydroxypropanes for

treating Alzheimer's disease)  
 RN 388063-46-5 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(3-iodophenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, mono(hydrochloride) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM (Continued)

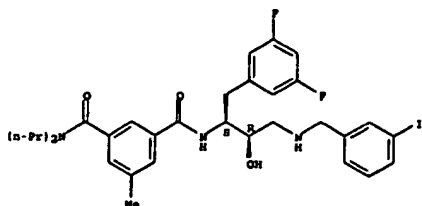


RN 388086-41-7 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(3-iodophenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CH 1

CN 388063-46-5  
 CN 388063-46-5

Absolute stereochemistry.



CH 2

CN 76-05-1  
 CN 76-05-1

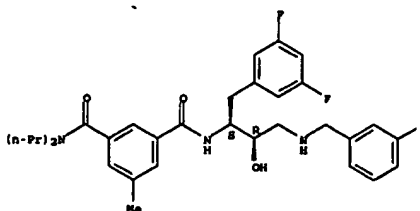


David

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM (Continued)

RN 597562-84-3 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(3-iodophenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, mono(hydrochloride) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



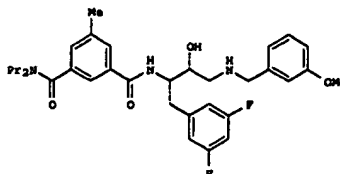
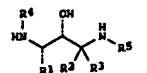
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05/11/2006

LA ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM  
 ACCESSION NUMBER: 200211402 CAPLUS  
 DOCUMENT NUMBER: 136:102190  
 TITLE: Preparation of substituted amines to treat Alzheimer's disease  
 INVENTOR(S): Maillaird, Michel; Hom, Court; Gallunas, Andres; Jagodinska, Barbara; Fang, Lawrence Y.; John, Varghese; Preskoe, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.  
 PATENT ASSIGNOR(S): Elian Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company  
 SOURCE: PCT Int. Appl., 451 pp.  
 CODEN: PEXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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KE 200200716	A	20040816	KE 2002-716	20010629
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			US 2000-255956P	P 20001215
			US 2001-268497P	P 20010213

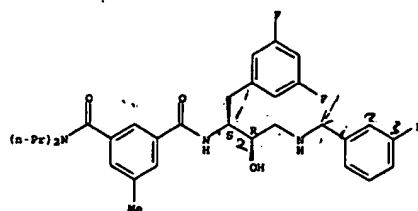
LA ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM (Continued)  
 US 2001-279779P P 20010329  
 US 2001-295589P P 20010604  
 EP 2001-950719 A3 20010629  
 WO 2001-US21012 W 20010629  
 OTHER SOURCE(S): MARPAT 136:102190  
 GI:



AB The title compds. (I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = H, (un)substituted alkyl, alkenyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.), useful in treating Alzheimer's disease and other similar diseases, were prepared. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-((3-methoxybenzyl)amino)-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC50 of < 50 μM against beta-secretase.  
 IT R1: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BICL (Biological study); PREP (Preparation); USES (Uses)

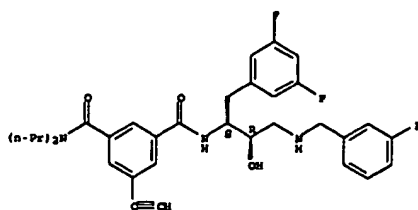
LA ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STM (Continued)  
 (prepn. of substituted amines for treating Alzheimer's disease)  
 RN 388063-46-5 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-5-methyl-N,N-dipropyl-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 388063-47-2 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-8-ethyl-N,N-dipropyl-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 388063-41-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of substituted amines for treating Alzheimer's disease)  
 RN 388063-41-7 CAPLUS  
 CN 1,3-Benzenedicarboxamide, N'-((1S,2R)-1-((3,5-difluorophenyl)methyl)-2-hydroxy-3-((3-iodophenyl)methyl)amino)propyl)-5-methyl-N,N-dipropyl-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CN 1

David

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10/143,502

Page 9

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

15.79

182.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-2.25

-2.25

STN INTERNATIONAL LOGOFF AT 11:38:18 ON 11 MAY 2006

Search Strategy for 10/143,502

=> d

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

RN 388063-46-5 REGISTRY

ED Entered STN: 30 Jan 2002

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(3-iodophenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide

FS STEREOSEARCH

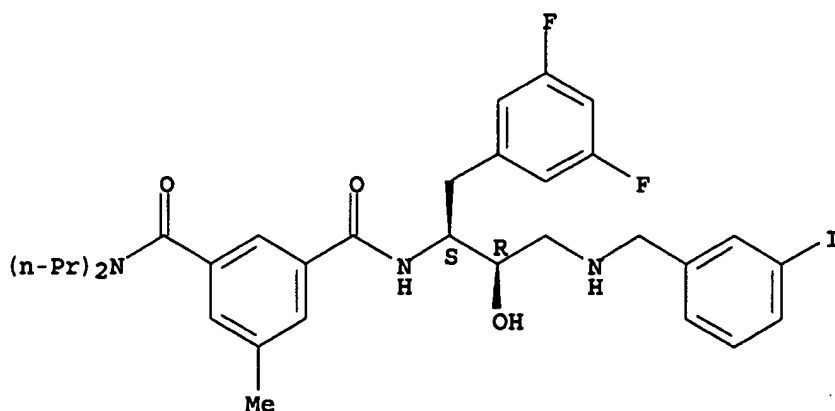
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CI COM

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)